

# Abstract

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## Clinical implications of discordance between low-density lipoprotein cholesterol and particle number

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**BACKGROUND:** The amount of cholesterol per low-density lipoprotein (LDL) particle is variable and related in part to particle size, with smaller particles carrying less cholesterol. This variability causes concentrations of LDL cholesterol (LDL-C) and LDL particles (LDL-P) to be discordant in many individuals.

**METHODS:** LDL-P measured by nuclear magnetic resonance spectroscopy, calculated LDL-C, and carotid intima-media thickness (IMT) were assessed at baseline in the Multi-Ethnic Study of Atherosclerosis, a community-based cohort of 6814 persons free of clinical cardiovascular disease (CVD) at entry and followed for CVD events ( $n = 319$  during 5.5-year follow-up). Discordance, defined as values of LDL-P and LDL-C differing by  $\geq 12$  percentile units to give equal-sized concordant and discordant subgroups, was related to CVD events and to carotid IMT in models predicting outcomes for a 1 SD difference in LDL-C or LDL-P, adjusted for age, gender, and race.

**RESULTS:** LDL-C and LDL-P were associated with incident CVD overall: hazard ratios (HR 1.20, 95% CI [CI] 1.08–1.34; and 1.32, 95% CI 1.19–1.47, respectively, but for those with discordant levels, only LDL-P was associated with incident CVD (HR 1.45, 95% CI 1.19–1.78; LDL-C HR 1.07, 95% CI 0.88–1.30). IMT also tracked with LDL-P rather than LDL-C, ie, adjusted mean IMT of 958, 932, and 917  $\mu\text{m}$  in the LDL-P > LDL-C discordant, concordant, and LDL-P < LDL-C discordant subgroups, respectively, with the difference persisting after adjustment for LDL-C ( $P = .002$ ) but not LDL-P ( $P = .60$ ).

**CONCLUSIONS:** For individuals with discordant LDL-C and LDL-P levels, the LDL-attributable atherosclerotic risk is better indicated by LDL-P.